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Parkinson’s disease: Alpha synuclein, heme oxygenase and biotherapeutic countermeasures

Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2018 Bentham Science Publishers. Neurodegenerative disorders have been and remain persistent sources of enormous suffering throughout human history. The tragedy of their impact on human relationships, physical vitality, and fundamental dignity cannot be understated. Parkinson’s disease (PD), one of the most common of these terrible illnesses, has a global incidence of approximately two-to-four percent of the human population, along with devastating social and economic impact. The present review analyzes aspects of PD pathophysiology that offer particularly attractive strategies for the development of improved prevention and therapy. The occurrence, symptoms, pathogenesis, and etiology of PD are considered, with focus on how the Alpha synuclein protein, which normally regulates neurotransmitter release, is aggregated by oxidative stressors into toxic inclusions, prominently including Lewy bodies and insoluble fibrils that disrupt the organization of brain areas responsible for motor control. The contribution to a progressively prooxidant tissue environment resulting from interaction between advanced glycation end products (AGEs) and their cognate receptors (RAGEs) is examined here as a significant driver of PD. This review also explores strategies currently being developed by a U.S.-Russian team that may reduce the risk and severity of PD by use of recombinant atoxic derivatives (ad) of botulinum neurotoxins (BoNT/A ad), that traffic inducers of the cytoprotective enzyme heme oxygenase to selected midbrain neurons, at which Alpha synuclein aggregation occurs. Considered together, the topic material presented here provides both researchers and clinicians with a short but concise overview of the current understanding of PD pathology and approaches to biotherapeutic (precision) countermeasures to its onset and progression.

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Keywords

Aggregation, Alpha synuclein, Heme oxygenase, Neurodegenerative disorders, Parkinson’s disease, Proteotoxic stress

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